

**REMARKS/ARGUMENTS**

Claim 1 has been amended. No new matter has been added by virtue of these amendments and their entry is respectfully requested. Claim 8 has been canceled without prejudice or disclaimer. Amendment and cancellation of the claims are not to be construed as an acquiescence to any of the rejections/objections set forth in the instant Office Action, and were done solely to expedite prosecution and allowance of the application. Applicants reserve the right to pursue the claims as originally filed, or substantially similar claims, in this or one or more continuation patent applications.

***Claim Rejections Under 35 U.S.C. §112***

Claims 1, 3, 5, 6, 8 and 14-18 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

In response, Applicants have amended claim 1 to recite that the cells are cultured for 5 days on a collagen coated plate. Support for this amendment is found on page 16, lines 17-23; see, also figure 2. Claims 3, 5, 6, and 8 depend from claim 1 and as such, include all the limitations of claim 1. The amended claims have explicit support in the specification and, as such, more than comply with 35 U.S.C. § 112, first paragraph.

Amendment and cancellation of the claims are not to be construed as an acquiescence to any of the rejections/objections set forth in the instant Office Action, and were done solely to expedite prosecution and allowance of the application. Applicants reserve the right to pursue the claims as originally filed, or substantially similar claims, in this or one or more continuation patent applications.

No new matter has been added by virtue of these amendments and their entry is respectfully requested. In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

Claims 1, 3, 5-6, 8 and 14-20 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement.

Applicants respectfully traverse. However, in order to expedite prosecution, Applicants have amended claim 1 to recite that the embryonic stem cells were cultured in hanging drops for 2 days to produce a culture of embryoid bodies. Support for this amendment is found, for example, page 13, lines 9-21. Amendment and cancellation of the claims are not to be construed as an acquiescence to any of the rejections/objections set forth in the instant Office Action, and were done solely to expedite prosecution and allowance of the application. Applicants reserve the right to pursue the claims as originally filed, or substantially similar claims, in this or one or more continuation patent applications.

No new matter has been added by virtue of these amendments and their entry is respectfully requested. In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

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***Claim Rejections Under 35 U.S.C. § 103 Liu/Keller***

Claims 1, 3, 8 and 14-19 are rejected under 35 U.S.C. § 103(a) as being unpatentable over WIPO document No. WO/10535 to Liu and Leahy, et al. (1999) *J. Exp. Zoo.*, 284:67-81.

Applicants respectfully traverse. However, in order to expedite prosecution, Applicants have amended claim 1 as discussed above. Neither Lui alone or in view of Leahy teach or disclose the instant invention which comprises providing an *in vitro* culture of embryonic stem cells (ES) cultured in hanging drops for 2 days to produce a culture of embryoid bodies, which are then divided into at least a first subculture and a second subculture and culturing the first and second subcultures for at least about 5 days in the absence of a test substance on a collagen coated culture plate; contacting the first subculture with a first test substance and a second

subculture with a second test substance; culturing the first and second subcultures for 7 to 18 days; and analyzing the cells in the first and second subcultures for increased tissue-specific gene expression. Claim 8 has been canceled, and dependent claims 3, and 14-19 incorporate the claim limitations of independent claim 1. Neither reference teaches the invention.

In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

Claims 1, 3, 5, 6, 8 and 14-19 are rejected under 35 U.S.C. § 103(a) as being unpatentable over WIPO document No. WO WO/10535 to Liu and Leahy, et al. (1999) *J. Exp. Zoo.*, 284:67-81, as applied to claim 1 above, and further in view of US Pat No 5,874,301 to Keller *et al.*

Applicants respectfully traverse. Applicants have amended claim 1 as discussed above. Neither Lui alone or in view of Leahy and Keller teach or disclose the instant invention which comprises providing an *in vitro* culture of embryonic stem cells (ES) cultured in hanging drops for 2 days to produce a culture of embryoid bodies, which are then divided into at least a first subculture and a second subculture and culturing the first and second subcultures for at least about 5 days in the absence of a test substance on a collagen coated culture plate; contacting the first subculture with a first test substance and a second subculture with a second test substance; culturing the first and second subcultures for 7 to 18 days; and analyzing the cells in the first and second subcultures for increased tissue-specific gene expression. Furthermore, Keller et al, teach the culturing of cells in the **presence of differentiating factors**. See for example col. 6., lines 39-64;

Thus, culturing of cells already differentiated would not make the invention obvious with respect to Lui in view of Leahy and Keller. Neither Keller nor Leahy make up for the deficiencies of Liu *et al.*

Claim 20 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Lui/Leahy or Lui/Leahy/Keller as applied to claim 1, above, and further in view of U.S. Patent No. 5,143,854 to Pirrung.

Applicants respectfully traverse. Applicants have discussed Lui/Leahy or Lui/Leahy/Keller as applied to claim 1. Claim 20 depends on amended claim 1 and as such, incorporates all the claim limitations of claim 1. Claim 1, as discussed is not rendered obvious by the cited references.

In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

### CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks and reconsideration and withdrawal of all rejections. It is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with the Applicants' attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at telephone number shown below.

Although, Applicants believe that no further extensions of time are required with submission of this paper, Applicants request that this submission also be considered as a petition for any further extension of time if necessary. The Commissioner for Patents and Trademarks is hereby authorized to charge the amount due for any retroactive extensions of time and any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees paid on the filing or during prosecution of this application to Deposit Account No. 50-0951.

Respectfully submitted,  
AKERMAN SENTERFITT



Nicholas A. Zachariades (Reg. No. 56,712)  
Akerman Senterfitt  
P.O. Box 3188  
West Palm Beach, FL 33402-3188  
Tel: 561-653-5000

Date: November 10, 2006

Docket No. 5853-207